

THAT WHICH IS CLAIMED IS:

1. A method for preparing an injectable formulation of interferon-beta (IFN- $\beta$ ) comprising:
- 5 a) preparing a first solution comprising IFN- $\beta$ , isolating a pool of purified IFN- $\beta$  from this solution, and precipitating said IFN- $\beta$  from this pool using an alcohol to form a precipitate;
- b) dissolving said precipitate in guanidine hydrochloride (HCl) to form a second solution comprising resolubilized denatured IFN- $\beta$  and guanidine HCl;
- 10 c) diluting said second solution into a first buffer to obtain a third solution comprising resolubilized renatured IFN-beta and residual guanidine HCl; and
- d) removing residual guanidine HCl from said third solution by diafiltration or dialysis of said third solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- $\beta$  is prepared.
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2. A pharmaceutical composition comprising substantially monomeric IFN- $\beta$  produced by the method of claim 1.
3. The method of claim 1, wherein said second buffer contains arginine or
- 20 sodium chloride.
4. The method of claim 1, wherein said first buffer has a pH of about 5.0 to about 8.0, and wherein said residual guanidine HCl is present in said third solution at a concentration of 1.6 M or less.
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5. A method for preparing an injectable formulation of interferon-beta (IFN- $\beta$ ), said method comprising denaturation of IFN- $\beta$  with guanidine hydrochloride (HCl) followed by renaturation of the IFN- $\beta$  via dilution into a first buffer to obtain a renatured IFN- $\beta$  solution comprising residual guanidine HCl, and removing said residual guanidine
- 30 HCl from said renatured IFN- $\beta$  solution by diafiltration or dialysis of said renatured IFN-

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β solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN-β is prepared.

5       6.       The method of claim 5, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said renatured IFN-β solution at a concentration of 1.6 M or less.

10       7.       The method of claim 6, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said renatured IFN-β solution at a concentration of 0.2 M or less.

15       8.       The method of claim 7, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN-β solution at a concentration of 0.1 M or less.

9.       A pharmaceutical composition comprising substantially monomeric IFN-β produced by the method of claim 5.

20       10.      A method for preparing a composition comprising substantially monomeric interferon-beta (IFN-β), said method comprising:  
a)       preparing a precipitate of substantially purified IFN-β;  
b)       dissolving said precipitate in guanidine hydrochloride (HCl) to obtain a first solution comprising resolubilized denatured IFN-β; and  
c)       renaturing said IFN-β by dilution of said first solution with a buffer  
25      solution.

11.      The method of claim 10, wherein said buffer solution has a pH of about 5.0 to about 8.0.

30       12.      A pharmaceutical composition comprising substantially monomeric IFN-β produced by the method of claim 10.

13. A method for preparing an injectable formulation of interferon-beta (IFN- $\beta$ ), said method comprising:

- a) obtaining a sample comprising substantially purified IFN- $\beta$ ;
- 5 b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- $\beta$ ;
- c) diluting said first solution into a first buffer to obtain a second solution comprising solubilized renatured IFN-beta and residual guanidine HCl; and
- d) removing residual guanidine HCl from said second solution by
- 10 diafiltration or dialysis of said second solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- $\beta$  is prepared.

14. A pharmaceutical composition comprising substantially monomeric IFN- $\beta$  produced by the method of claim 13.

15. The method of claim 13, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 1.6 M or less.

20 16. The method of claim 15, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 0.2 M or less.

25 17. The method of claim 16, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 0.1 M or less.

18. A method for preparing a composition comprising substantially monomeric interferon-beta (IFN- $\beta$ ), said method comprising:

- 30 a) preparing a sample comprising substantially purified IFN- $\beta$ ;

b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- $\beta$ ; and

c) renaturing said IFN- $\beta$  by dilution of said first solution with a buffer solution.

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19. The method of claim 18, wherein said buffer solution has a pH of about 3.0 to about 5.0.

20. A pharmaceutical composition comprising substantially monomeric IFN- $\beta$   
10 produced by the method of claim 18.

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